

WHAT IS CLAIMED IS:

1. A method to identify an ISG15 target protein, comprising:
  - (a) contacting a sample with an antibody, wherein the sample is suspected of having a conjugate comprising ISG15 and a target protein under conditions that permit the antibody to bind the conjugate; and
  - (b) detecting the target protein of the bound conjugate, wherein the target protein is an ISG15 target protein.
2. The method of claim 1, wherein step (a) comprises:
  - (a) contacting the sample with a first antibody that binds to the conjugate to form a first complex; and
  - (b) contacting the conjugate with a second antibody that binds to the conjugate to form a second complex.
3. The method of claim 2, wherein the first antibody is separated from the conjugate prior to contacting the conjugate with the second antibody.
4. The method of claim 2, wherein the first antibody binds to ISG15 when bound to the target protein and the second antibody binds to the target protein when bound to ISG15.
5. The method of claim 2, wherein the first antibody binds to the target protein when bound to ISG15 and the second antibody binds to ISG15 when bound to the target protein.

6. The method of claim 1, wherein the antibody selectively binds to the conjugate.
7. The method of claim 1, wherein the sample is a physiological sample obtained from a mammal.
8. The method of claim 7, wherein the mammal is a human.
9. The method of claim 7, wherein the sample is from thymus.
10. The method of claim 1, further comprising separating unconjugated ISG15 from the sample prior to contacting the sample with the antibody.
11. The method of claim 10, wherein the unconjugated ISG15 is removed from the sample by gel filtration chromatography.
12. The method of claim 11, wherein the unconjugated ISG15 is removed from the sample by gel filtration chromatography on Sephadex G-50.
13. The method of claim 1, wherein the sample is prepared *in vitro* by combining ISG15, an ISG15 activator enzyme, and an ISG15 target protein to form a conjugate comprising ISG15 and the target protein.
14. The method of claim 1, wherein the ISG15 target protein is detected by western blot.
15. The method of claim 6, wherein the antibody is a monoclonal antibody.

16. The method of claim 2, wherein the first antibody is selected from the group consisting of a monoclonal antibody and a polyclonal antibody.
17. The method of claim 2, wherein the second antibody comprises a monoclonal antibody and a polyclonal antibody.
18. The method of claim 2, wherein the second antibody comprises a mixture of antibodies that bind to the target protein when bound to ISG15.
19. The method of claim 2, wherein the first antibody is immobilized.
20. A method to identify an ISG15 target protein, comprising:
  - (a) isolating a conjugate comprising ISG15 and a target protein; and
  - (b) identifying the target protein.
21. The method of claim 20, wherein the conjugate of ISG15 and a target protein is isolated through use of an antibody, or liquid chromatography.
22. The method of claim 20, wherein mass spectrometry is used to detect the target protein.
23. The method of claim 20, further comprising separating ISG15 from the target protein.
24. The method of claim 23, wherein UBP43 is used to separate ISG15 from the target protein.

25. A method to identify a compound that alters the conjugation of ISG15 with a target protein, comprising:
- (a) contacting a sample comprising ISG15, an ISG15 activating enzyme, and an ISG15 target protein with a compound;
  - (b) detecting the amount of the conjugate in the sample; and
  - (c) comparing the amount of conjugate detected in step (b) with a control amount of conjugate, as determined from a sample not contacted with the compound, wherein a difference in the amount of conjugate detected in step (b) and the control amount indicates that the compound alters the conjugation of ISG15 with the target protein.
26. The method of claim 25, wherein the detection step further comprises:
- (a) contacting the sample with a first antibody that binds to the conjugate to form a first complex; and
  - (b) contacting the conjugate with a second antibody that binds to the conjugate of ISG15 and the target protein to form a second complex.
27. The method of claim 26, wherein the first antibody is separated from the conjugate prior to contacting the conjugate with the second antibody.
28. The method of claim 26, wherein the first antibody binds to ISG15 when bound to the target protein and the second antibody binds to the target protein when bound to ISG15.

29. The method of claim 26, wherein the first antibody binds to the target protein when bound to ISG15 and the second antibody binds to the ISG15 when bound to the target protein.
30. The method of claim 25, wherein the amount of conjugate is detected by contacting the sample with an antibody that selectively binds to the conjugate.
31. The method of claim 25, wherein the sample is a physiological sample obtained from a mammal.
32. The method of claim 31, wherein the mammal is a human.
33. The method of claim 31, wherein the sample is from thymus.
34. The method of claim 25, further comprising separating unconjugated ISG15 from the sample prior to detecting the amount of conjugate in the sample.
35. The method of claim 34, wherein the unconjugated ISG15 is removed from the sample by gel filtration chromatography.
36. The method of claim 35, wherein the unconjugated ISG15 is removed from the sample by gel filtration chromatography on Sephadex G-50.
37. The method of claim 25, wherein the sample is prepared *in vitro*.
38. The method of claim 25, wherein the ISG15 target protein is detected by western blot.

39. The method of claim 30, wherein the antibody is selected from the group consisting of a monoclonal antibody and a polyclonal antibody.
40. The method of claim 26, wherein the first antibody is selected from the group consisting of a monoclonal antibody and a polyclonal antibody.
41. The method of claim 26, wherein the second antibody is selected from the group consisting of a monoclonal antibody or a polyclonal antibody.
42. The method of claim 26, wherein the second antibody comprises a mixture of antibodies that bind to the target protein when bound to ISG15.
43. The method of claim 26, wherein the first antibody is immunobilized.
44. The method of claim 25, wherein the sample further comprises UBP43.
45. A composition comprising an isolated ISG15-conjugate.
46. The composition of claim 45, wherein the ISG15-conjugate is selected from the group consisting of an ISG15-phospholipase PLC $\gamma$ 1 conjugate, an ISG15-Jak1 conjugate, an ISG15-ERK1 conjugate, an ISG15-ERK2 conjugate, an ISG15-Stat1 conjugate, a variant thereof, and a combination thereof.
47. The composition of claim 45, further comprising a pharmaceutically acceptable carrier.

48. A method to diagnose a patient having a malcondition characterized by an altered level of ISG15-conjugated protein, comprising:
- (a) contacting an antibody that selectively binds an ISG15-conjugated protein with a sample from the patient suspected of having an ISG15-conjugated protein; and
  - (b) detecting the level of ISG15-conjugated protein in the sample, wherein an alteration in the level of ISG15-conjugated protein, as compared to the level of ISG15-conjugated protein in a patient not having the malcondition, indicates that the patient has the malcondition.
49. The method of claim 48, wherein step (a) comprises:
- (a) contacting the sample with a first antibody that binds to the conjugate to form a first complex; and
  - (b) contacting the conjugate with a second antibody that binds to the conjugate to form a second complex.
50. The method of claim 49, wherein the first antibody is separated from the conjugate prior to contacting the conjugate with the second antibody.
51. The method of claim 49, wherein the first antibody binds to ISG15 when bound to the target protein and the second antibody binds to the target protein when bound to ISG15.
52. The method of claim 49, wherein the first antibody binds to the target protein when bound to ISG15 and the second antibody binds to the ISG15 when bound to the target protein.

53. The method of claim 48, wherein the antibody selectively binds to the conjugate.
54. The method of claim 48, wherein the sample is from thymus.
55. The method of claim 48, further comprising separating unconjugated ISG15 from the sample prior to contacting the sample with the antibody.
56. The method of claim 55, wherein the unconjugated ISG15 is removed from the sample by gel filtration chromatography.
57. The method of claim 56, wherein the unconjugated ISG15 is removed from the sample by gel filtration chromatography on Sephadex G-50.
58. The method of claim 48, wherein the ISG15 target protein is detected by western blot.
59. The method of claim 58, wherein the antibody comprises a monoclonal antibody.
60. The method of claim 49, wherein the first antibody is selected from the group consisting of a monoclonal antibody and a polyclonal antibody.
61. The method of claim 49, wherein the second antibody is selected from the group consisting of a monoclonal antibody and a polyclonal antibody.
62. The method of claim 49, wherein the second antibody comprises a mixture of antibodies that bind to the target protein when bound to ISG15.



63. The method of claim 48, wherein the first antibody is an immobilized antibody.
64. An antibody that selectively binds to an ISG15-conjugate, wherein the ISG15-conjugate comprises ISG15 and an ISG15 conjugated protein, wherein the antibody does not selectively bind to ISG15 alone, and wherein the antibody does not selectively bind to the ISG15 conjugated protein alone.
65. The antibody of claim 64, wherein the antibody selectively binds to an ISG15-conjugate selected from the group consisting of ISG15-phospholipase PLC $\gamma$ 1 conjugate, an ISG15-Jak1 conjugate, an ISG15-ERK1 conjugate, an ISG15-ERK2 conjugate, and an ISG15-Stat1 conjugate.
66. The antibody of claim 65, wherein the antibody is a monoclonal antibody.
67. A method to inhibit cell proliferation comprising contacting a cell with a composition comprising an ISG15-conjugate.
68. The method of claim 67, wherein the ISG15-conjugate is selected from the group consisting of an ISG15-phospholipase PLC $\gamma$ 1 conjugate, an ISG15-Jak1 conjugate, an ISG15-ERK1 conjugate, an ISG15-ERK2 conjugate, an ISG15-Stat1 conjugate, a variant thereof, and a combination thereof.
69. The method of claim 67, wherein the disorder related to cellular proliferation is cancer.
70. The method of claim 69, wherein the cancer is leukemia.

71. The method of claim 67, further comprising contacting the cell with retinoic acid.
72. A method to increase the intracellular concentration of an ISG15-conjugate comprising contacting the cell with a composition comprising the ISG15-conjugate.
73. The method of claim 72, wherein the ISG15-conjugate is selected from the group consisting of an ISG15-phospholipase PLC $\gamma$ 1 conjugate, an ISG15-Jak1 conjugate, an ISG15-ERK1 conjugate, an ISG15-ERK2 conjugate, an ISG15-Stat1 conjugate, a variant thereof, and a combination thereof.
74. A method to increase migration of a cell comprising contacting the cell, or a surface on which the cell migrates, with a composition comprising an ISG15-conjugate.
75. The method of claim 74, wherein the ISG15-conjugate is selected from the group consisting of an ISG15-phospholipase PLC $\gamma$ 1 conjugate, an ISG15-Jak1 conjugate, an ISG15-ERK1 conjugate, an ISG15-ERK2 conjugate, an ISG15-Stat1 conjugate, a variant thereof, and a combination thereof.
76. A method to increase phagocytotic activity of a cell comprising contacting the cell, or a surface on which the cell migrates, with a composition comprising an ISG15-conjugate.

77. The method of claim 76, wherein the cell is at the site of a wound.
78. The method of claim 76, wherein the ISG15-conjugate is selected from the group consisting of an ISG15-phospholipase PLC $\gamma$ 1 conjugate, an ISG15-Jak1 conjugate, an ISG15-ERK1 conjugate, an ISG15-ERK2 conjugate, an ISG15-Stat1 conjugate, a variant thereof, and a combination thereof.
79. A method to increase wound healing comprising contacting a wound with a composition comprising an ISG15-conjugate.
80. The method of claim 79, wherein the ISG15-conjugate is selected from the group consisting of an ISG15-phospholipase PLC $\gamma$ 1 conjugate, an ISG15-Jak1 conjugate, an ISG15-ERK1 conjugate, an ISG15-ERK2 conjugate, an ISG15-Stat1 conjugate, a variant thereof, and a combination thereof.
81. A method to determine the responsiveness of a patient to treatment with an interferon, comprising:
- (a) administering an interferon to the patient suspected of being responsive to interferon treatment;
  - (b) determining the amount of ISG-15-conjugated protein in the patient;  
and
  - (c) comparing the amount of ISG-15-conjugated protein in the patient before and after administration of the interferon,  
wherein an increase in ISG15-conjugated protein indicates greater responsiveness to interferon treatment.

82. An ISG15-conjugate selected from the group consisting of ISG15-Stat1, ISG15-ERK1, ISG15-ERK2, ISG15-PLC $\gamma$ 1, and ISG15-Jak1.
83. An isolated complex comprising an ISG15-conjugate and an antibody that selectively binds to the conjugate.
84. The complex of claim 84, wherein the ISG15-conjugate is selected from the group consisting of an ISG15-phospholipase PLC $\gamma$ 1 conjugate, an ISG15-Jak1 conjugate, an ISG15-ERK1 conjugate, an ISG15-ERK2 conjugate, an ISG15-Stat1 conjugate, a variant thereof, and a combination thereof.
85. A method to increase the intracellular concentration of an ISG15-conjugate comprising contacting the cell with a composition comprising the compound identified according to the method of claim 25.
86. A method to inhibit cell proliferation comprising contacting a cell with a composition comprising the compound identified according to the method of claim 25.
87. A method to increase migration of a cell comprising contacting the cell, or a surface on which the cell migrates, with a composition comprising the compound identified according to the method of claim 25.
88. A method to increase phagocytotic activity of a cell comprising contacting the cell, or a surface on which the cell migrates, with a composition comprising the compound identified according to the method of claim 25.

89. A method to increase wound healing comprising contacting a wound with a composition comprising the compound identified according to the method of claim 25.